

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/GB05/001290

International filing date: 04 April 2005 (04.04.2005)

Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/573,468
Filing date: 21 May 2004 (21.05.2004)

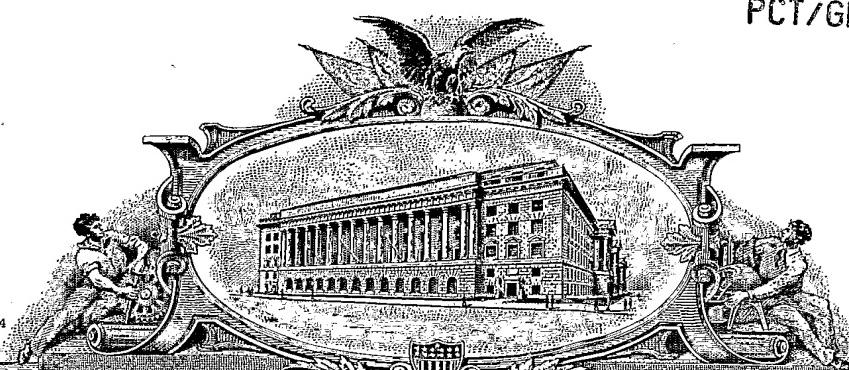
Date of receipt at the International Bureau: 12 May 2005 (12.05.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)



World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse

PA 1303614



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

April 06, 2005

**THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM
THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK
OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT
APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A
FILING DATE UNDER 35 USC 111.**

APPLICATION NUMBER: 60/573,468

FILING DATE: May 21, 2004

**By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS**



W. MONTGOMERY
Certifying Officer

Please type a plus sign inside this box

PTO/SB/16 (02-01)

Approved for use through 10/31/2002. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE**PROVISIONAL APPLICATION FOR PATENT COVER SHEET**

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. **EL908623385US** United States Postal Service "USPS"I hereby certify that this correspondence is being deposited with the USPS as
Express Mail under 37 CR 1.10Print Name: *PAUL DIUTTO*
*Paul Diutto*11548 U.S.P.T.O.
60/573468

052104

INVENTOR(S)

Given Name (first and middle [if any]) Kevin	Family Name or Surname Giles	Residence (City and either State or Foreign Country) 16 North Vale Road, Timperley, Altrincham, Cheshire WA15 7RR United Kingdom
		Citizenship: UK

Additional inventors are being named on the **2** separately numbered sheets attached hereto**TITLE OF THE INVENTION (280 characters max)****TITLE****MASS SPECTROMETER**

<i>Direct all correspondence to:</i>		CORRESPONDENCE ADDRESS		
<input type="checkbox"/> Customer Number		<input type="checkbox"/> Customer Number		
OR				
<input checked="" type="checkbox"/> Firm or Individual Name	Anthony J. Janiuk, Esq. – Reg. No. 29,809 Lin B. Olsen, Esq. – Reg. No. 41,230			
Address	Waters Corporation 34 Maple Street – MS: LG			
City	Milford	State	MA	Zip 01757
Country	USA	Telephone	(508) 482-2714	Fax (508) 482-2320
ENCLOSED APPLICATION PARTS (check all that apply)				
<input checked="" type="checkbox"/>	Specification & Claims Number of Pages	40	CD(s), Number	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Drawing(s) Number of Sheets	16	<input checked="" type="checkbox"/> Other:	Prepaid Return Postcard
<input checked="" type="checkbox"/>	Application Data Sheet. See 37 CFR 1.76			

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT				
<input checked="" type="checkbox"/> Applicant claims large entity status.				
<input type="checkbox"/> A check or money order is enclosed to cover the filing fees	FILING FEE AMOUNT (\$)			
<input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number:	23-0503		160.00	
The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.				
<input checked="" type="checkbox"/> No	<input type="checkbox"/> Yes, the name of the U.S. Government agency and the Government contract number are:			

Respectfully submitted

SIGNATURE

TYPED OR
PRINTED NAME*Anthony J. Janiuk*

TELEPHONE

(508) 482-2 Fax: (508) 482-2320

Date **May 21, 2004**

REGISTRATION NO.

(If appropriate) **29,809**

Docket Number:

AE-MM-14

Docket No. AE-MM-14
(1329 US1)
Express Mail No. EL908623385US

PROVISIONAL APPLICATION PATENT COVER SHEET

SECOND PAGE

ADDITIONAL INVENTORS:

Martin Green, Grange Croft, Grange Road, Bowden, Altrincham,
Cheshire WA14 3EE, United Kingdom
Citizenship: UK

Steve Pringle, Linden Cottages, Temple Hoddlesden, Darwen, BB3 3PS, United
Kingdom
Citizenship: UK

Jason Lee Wildgoose, 110 Baricroft Road, Heaton Mersey, Stockport, SK4 3PJ
United Kingdom
Citizenship: UK

Waters

Docket No. AE-MM-14
(MST 1329 US1)

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
(37 CFR § 1.10) No. EL 908623385 US

TITLE OF INVENTION:

MASS SPECTROMETER

INVENTOR(S): Kevin Giles, Martin Green, Steve Pringle and Jason Lee Wildgoose

FILING DATE: HEREWITH

ASSIGNEE: Micromass UK Limited

APPLICATION NUMBER (to be assigned)

MAIL STOP- PROVISIONAL APPLICATION
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I hereby certify that the correspondence identified in the transmittal below is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR § 1.10 in an envelope addressed to: Mail Stop Provisional Applications, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on May 21, 2004.

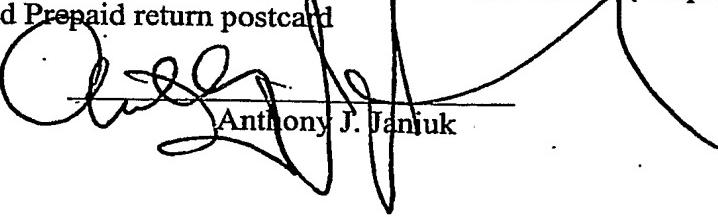
Paul DiVitto
Paul DiVitto

TRANSMITTAL LETTER

Enclosed for filing in the above identified patent case are the following documents:

Certificate of Mailing under 37 CFR § 1.10, Transmittal Letter, Provisional Transmittal (2 pg.); Title page (1 pg), Applicant Data Sheet, Specifications and claims (40 pages), Drawings (16 sheets) and Prepaid return postcard

May 21, 2004
Reg. No. 29,809


Anthony J. Janjuk

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

U.S. PROVISIONAL PATENT APPLICATION

ENTITLED:

MASS SPECTROMETER

INVENTOR(S):

Kevin Giles

Martin Green

Steve Pringle

Jason Lee Wildgoose

APPLICATION DATA SHEET

APPLICATION INFORMATION

Application Type: Regular
Subject Matter: Utility
Title: MASS SPECTROMETER
Attorney Docket No. AE-MM-14 (MST-1329 US1)
Request for Early Publication: No
Request for Non-Publication: No
Large Entity Yes

APPLICANT INFORMATION

Application Authority Type: Inventor
Primary Citizenship Country: UK
Status: Full Capacity

First Name: Kevin

Family Name: Giles

Street of mailing address: 16 North Vale Road
Timperley
Altrincham
Cheshire
WA14 3EE

Country of mailing address: United Kingdom

Application Authority Type: Inventor
Primary Citizenship Country: UK
Status: Full Capacity

Given Name: Martin

Family Name:	Green
Street of mailing address:	Grange Croft Linden Cottages Temple Hoddesden Darwen, BB3 3PS United Kingdom
Country of Residence:	
Application Authority Type:	Inventor
Primary Citizenship Country:	UK
Status:	Full Capacity
Given Name:	Steve
Family Name:	Pringle
Street of mailing address:	Linden Cottages Temple Hoddesden Darwen BB3 3PS United Kingdom
Country of Residence:	
Application Authority Type:	Inventor
Primary Citizenship Country:	UK
Status:	Full Capacity
Given Name:	Jason
Middle Name:	Lee
Family Name:	Wildgoose
Street of mailing address:	110 Barcicroft Road Heaton Mersey Stockport SK4 3PJ United Kingdom
Country of Residence:	

CORRESPONDENCE INFORMATION

Agent for Applicant: Anthony J. Janiuk
Registration No. 29,809
Company Name: Waters Corporation
Street of mailing address: 34 Maple Street
City & State of mailing address: Milford, Massachusetts
Postal Zip Code: 01757
Telephone (508) 482-2714
Facsimile (508) 482-2320
Email anthony_janiuk@waters.com

ASSIGNEE INFORMATION

Name of Company: Micromass UK Limited
Street address: Atlas Park
Simonsway, Manchester
M22 5PP
Country: United Kingdom
Company formed: United Kingdom

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail: EL908623385US

5

MASS SPECTROMETER

The present invention relates to a mass spectrometer and a method of mass spectrometry.

In many mass spectrometric applications very complex mixtures of compounds are analysed. Individual components within these mixtures may be present with a wide range of relative concentrations. This can give rise to a wide range of ion current intensities which are transmitted to the mass analyser and the ion detector. For many of these applications it is important to produce quantitative and qualitative data (in the form of exact mass measurement) for as many components as possible. This can place very high demands upon the dynamic range of the mass analyser and the detection system employed in the mass spectrometer.

One method which has been employed to extend the dynamic range for quantitative and qualitative analysis is to adjust the intensity of the ion beam transmitted to the mass analyser by a pre-determined factor. This ensures that mass spectral data is then only recorded when the ion beam received by the mass analyser does not cause saturation of the mass analyser or ion detector.

In general, known ways of reducing the intensity of an ion beam use either a focusing or deflecting electrostatic lens upstream of a plate having an aperture. The profile of the ion beam may be expanded by the electrostatic lens or the ion beam may be deflected in a direction away from the initial direction of the ion beam such that only a portion of the ion beam is transmitted through the aperture in the plate. The remaining ions strike the surface of the plate. For

example, a known arrangement increases the dynamic range by attenuating an ion beam in a low transmission mode of operation by defocusing the ion beam such that the profile of the ion beam exceeds that of an aperture of
5 an exit slit arranged downstream of an Einzel lens. Accordingly, in the low transmission mode of operation only a fraction of the ions pass through the aperture of the exit slit arranged downstream of the Einzel lens whilst the remaining ions strike the surface of the exit
10 electrode. The reduced intensity ion beam is then mass analysed. As an alternative to defocusing the ion beam it is also known to deflect the ion beam to one side such that in a low transmission mode of operation most of the ion beam impinges upon the exit slit and only a
15 small proportion of the ion beam is transmitted past the exit electrode. However, the conventional methods of either defocusing or deflecting an ion beam using an Einzel lens arrangement to reduce the transmission of an ion beam suffer from a number of problems.

20 Firstly, it is difficult to precisely operate the known Einzel lens arrangement in a conventional manner such that the desired attenuation of the ion transmission is precisely achieved. Generally, the Einzel lens arrangement must first be calibrated by
25 measuring the transmission of the Einzel lens system at several different lens conditions in order to empirically determine the relationship between the voltages applied to the Einzel lens and relative transmission of the Einzel lens. However, this
30 relationship may also depend upon the settings of other focussing elements in the system. Consequently, it is necessary to recalibrate the Einzel lens at regular

intervals in order to ensure an accurate estimation of the relative transmission.

Secondly, the portion of the ion beam which is not allowed to pass through the aperture of the exit slit 5 strikes the surface of the exit slit predominantly in the region surrounding the aperture in the exit slit. This can cause surface charging around the aperture in the exit slit. As a result an additional potential due to surface charging effects may be present around the 10 aperture in the exit slit which may interfere with ions being transmitted through the exit slit. This can lead to changes in the focussing of the ion beam and as a result the ratio between the high and low transmission modes of operation may suffer from instability.

15 Thirdly, the conventional approach of defocusing or deflecting the ion beam can alter the cross-sectional profile of the ion beam, the spatial and angular distributions of the ion beam and the velocity or energy profile of the ion beam. This can affect the 20 performance, mass resolution and mass calibration of a mass analyser which mass analyses the ion beam.

Fourthly, if the cross sectional profile of the ion beam passing through the Einzel lens varies as a function of mass to charge ratio, then the relative 25 transmission between high and low transmission modes of operation may be different for ions having different mass to charge ratios. This may cause an additional complication in calibrating the effect of the attenuation across a wide range of mass to charge 30 ratios. For example, the cross sectional profile of an ion beam exiting an Electron Impact ("EI") ion source or a Chemical Ionisation ("CI") ion source may vary with respect to mass to charge ratio due to the mass

dispersing action of stray magnetic field from magnets employed to focus the ionising electron beam in the ionisation source. As another example, an ion transfer device utilising RF voltages may have transmission and 5 focussing properties which are dependent upon the mass to charge ratio of ions.

It is therefore desired to provide an improved mass spectrometer and method of mass spectrometry.

According to the present invention, there is 10 provided a mass spectrometer as claimed in claim 1.

The preferred embodiment relates to a way of attenuating a continuous ion beam by rapidly gating the transmission of ions between low, preferably zero transmission and high (or full) transmission through an 15 ion beam attenuator. A particularly advantageous feature of the preferred embodiment is that the degree of attenuation can preferably be precisely controlled and predicted by varying the time spent by the ion beam attenuator in either the zero or high (e.g. full) 20 transmission modes.

In a preferred embodiment the ion transmission is adjusted using a pulsed ion gate or ion beam attenuator. During a low transmission mode the ion gate is preferably closed and hence preferably no ions pass 25 through or exit from the ion gate i.e. the attenuation factor is substantially 100%. During a subsequent period during which the ion gate is open preferably a large proportion of the ion beam passes through or exits from the ion gate and hence the ion gate has high or 30 full transmission i.e. the attenuation factor may be very low or preferably 0%. By changing the mark space ratio of the ion beam attenuator between the two

transmission modes the average flux of ions through the system may be precisely adjusted.

The preferred method of controlling the transmission or attenuation of an ion beam preferably 5 overcomes various problems associated with the conventional methods. In particular, the attenuation factor by which the transmission of ions is reduced may be precisely controlled and predicted. The relative transmission is also directly proportional to the duty 10 cycle of the gating pulse or ion gate, and this negates any requirement for calibration of the attenuating characteristics of the device.

The preferred ion beam attenuator is also preferably arranged such that during a zero (or low) 15 transmission mode of operation ions are directed away from and preferably do not impinge upon surfaces which are in close proximity to the ion beam when the ion beam attenuator is in a subsequent high or full transmission mode i.e. the ion beam is preferably arranged so as not 20 to impact around an aperture in an exit slit through which ions are subsequently transmitted in a high transmission mode of operation. This significantly reduces surface charging effects which can otherwise adversely effect the focussing (and hence transmission) 25 of the ion beam particularly in a high (or full) transmission mode of operation.

According to the preferred embodiment the ion beam is only transmitted under high or full transmission conditions. Under these conditions the gating device or 30 ion beam attenuator is effectively inactive. Thus the overall transmission resulting from switching the ion beam attenuator between modes may preferably be reduced without introducing significant spatial aberrations and

without introducing energy spread of the ion beam as may be associated with conventional arrangements.

- Since the ion beam is preferably only transmitted under high or full transmission conditions where the
5 gating device or ion beam attenuator is preferably inactive, the preferred embodiment results in an ion beam attenuator which has a constant attenuation factor with respect to mass to charge even if the ion beam is inhomogeneous with respect to mass to charge ratio.
10 This is a particularly advantageous aspect of the preferred embodiment.

Various embodiments of the present invention will now be described, by way of example only, and with reference to the accompanying drawings in which:

- 15 Fig. 1 shows a conventional Einzel lens arrangement in a high transmission mode of operation;

Fig. 2 shows a conventional Einzel lens arrangement in a low transmission mode of operation wherein the ion beam is defocused;

- 20 Fig. 3 shows a conventional Einzel lens arrangement in an alternative low transmission mode of operation wherein the ion beam is deflected;

- Fig. 4 shows a zero transmission mode of operation according to an embodiment of the present invention
25 wherein a retarding potential is applied to an electrode of an ion gate or ion beam attenuator;

Fig. 5 shows a preferred ion gate or ion beam attenuator in a high transmission mode of operation;

- Fig. 6 shows a voltage timing diagram illustrating
30 the time during which a retarding voltage pulse is applied to an ion gate or ion beam attenuator according to a preferred embodiment;

Fig. 7 shows an attenuative zero transmission mode of operation according to an embodiment of the present invention wherein a deflecting potential is applied to an electrode of an ion gate or ion beam attenuator;

5 Fig. 8 shows a SIMION (RTM) model of a preferred ion gate or ion beam attenuator in a high transmission mode of operation;

10 Fig. 9 shows a 3D potential energy diagram of the potentials within the preferred ion gate or ion beam attenuator in the high transmission mode of operation as shown in Fig. 8;

15 Fig. 10 shows a SIMION (RTM) model of a preferred ion gate or ion beam attenuator in a zero transmission mode of operation;

Fig. 11 shows a 3D potential energy diagram of the potentials within the preferred ion gate or ion beam attenuator in the zero transmission mode of operation as shown in Fig. 10;

20 Fig. 12 shows an experimentally determined relationship between the relative transmission of an ion beam attenuator according to a preferred embodiment versus the duty cycle of the ion beam attenuator;

25 Fig. 13 shows the same data as shown in Fig. 12 but plotted on a log-log scale for sake of clarity;

Fig. 14A shows a mass spectrum obtained at 100% ion transmission with an Electrospray ion source and Fig. 14B shows a corresponding mass spectrum obtained when an ion beam attenuator according to the preferred embodiment was used to attenuate the ion beam by 90%;
30 and

Fig. 15A shows a portion of the mass spectrum shown in Fig. 14A in greater detail and Fig. 15B shows a

portion of the mass spectrum shown in Fig. 14B in greater detail.

A conventional Einzel lens arrangement is shown in Fig. 1 wherein the Einzel lens arrangement is in a high transmission mode of operation. As such, a beam of positive ions 1a is transmitted by the Einzel lens arrangement substantially without being attenuated i.e. the ion beam transmission is 100% and the attenuation factor is 0%. The Einzel lens arrangement comprises an electrostatic lens assembly comprising first electrodes 2a,2b, second electrodes 3a,3b and third electrodes 4a,4b. An exit slit or electrode 5 is also provided downstream of the third electrodes 4a,4b. In a high transmission mode of operation the first, second and third electrodes 2a,2b,3a,3b,4a,4b are held at nominally identical voltages such that an essentially field free region is provided within the Einzel lens arrangement. The ion beam is fully transmitted through the exit slit or electrode 5 and hence the ion beam 1b which emerges from the Einzel lens arrangement has substantially the same intensity as the ion beam 1a which was initially received by the Einzel lens arrangement.

Fig. 2 shows the same Einzel lens arrangement as shown in Fig. 1 but operated in a low transmission mode of operation wherein the second electrodes 3a,3b of the Einzel lens arrangement are now supplied with a voltage which is above that of the voltages applied to the first and third electrodes 2a,2b,4a,4b (and also the exit slit or electrode 5). As a result the ion beam 1 passing through the Einzel lens arrangement is substantially defocused. A large proportion of the ion beam impinges upon the exit slit or electrode 5 and only a small proportion of the ion beam passes through the exit slit

or electrode 5. Accordingly, in this mode of operation the ion transmission is reduced by a certain amount e.g. the ion beam 1b which emerges from the Einzel lens arrangement may, for example, be attenuated by 90%. As 5 can be seen from Fig. 2 in the low transmission mode of operation a significant proportion of the ion beam impinges upon the front surface of the exit slit or electrode 5 in a region close to or immediately surrounding the opening or aperture in the exit slit or 10 electrode 5. As discussed above, an ion beam impinging upon the exit slit or electrode 5 can cause surface charging effects which can affect the subsequent transmission of ions through the exit slit or electrode 5 particularly in a subsequent high transmission mode of 15 operation.

Fig. 3 shows an Einzel lens arrangement operated in an alternative low transmission mode of operation wherein the two electrodes 3a,3b forming the second electrodes are maintained at different relative voltages. In the arrangement shown in Fig. 3 one of the second electrodes 3a is raised to a voltage which is above that of the voltage applied to the other second electrode 3b and which is also above the voltage applied to the first and third electrodes 2a,2b,4a,4b and the 20 exit slit or electrode 5. The ion beam is, as a result, deflected away from the second electrode 3a to which a high voltage is applied by the raised potential on that electrode 3a. As a result the majority of the ion beam is deflected so as to impinge upon the exit slit or 25 electrode 5 but a small proportion of the ion beam is onwardly transmitted by the exit slit or electrode 5. However, as can be seen from Fig. 3 the ion beam 1b 30 which is onwardly transmitted is substantially off-axis

or inclined to the direction of travel of the ion beam 1a received by the Einzel lens arrangement.

In the low transmission mode of operation shown in Fig. 3 the ion beam may, for example, be attenuated by 5 90%. The remainder of the ion beam is incident upon the front surface of the exit slit or electrode 5 in very close proximity to the opening or aperture in the exit slit or electrode 5. The detrimental effects due to surface charging of the exit slit or electrode 5 can 10 therefore be particularly problematic with this particular arrangement and mode of operation.

As will be appreciated one of the problems with the conventional modes of operating an Einzel lens arrangement to attenuate an ion beam is that a 15 significant proportion of the ion beam will impinge upon an exit slit or electrode 5 in a way such that surface charging effects in a region adjacent to an opening or aperture in the exit slit or aperture 5 are likely to adversely affect the subsequent performance of the 20 Einzel lens arrangement especially when the lens is switched to a high transmission mode of operation.

A preferred embodiment of the present invention will now be described with reference to Fig. 4. A beam of positive ions 1 is shown traversing an electrostatic 25 lens assembly arranged and operated according to a preferred embodiment. The preferred lens arrangement comprises first electrodes 2a,2b, second electrodes 3a,3b, third electrodes 4a,4b and an exit slit or electrode 5. The second electrodes 3a,3b preferably 30 have a radial separation which is greater than the first and second electrodes and which may be comparable to the radial separation of the exit slit 5 or the diameter of an aperture in the exit slit 5. At a first time T1 a

gate or retarding voltage is preferably applied to the third electrodes 4a,4b. The gate or retarding voltage preferably causes the entire ion beam to be reflected or retarded in such a way that the ions are accelerated in 5 an opposite direction to their initial direction of travel. The reflected ions are preferably arranged to fall incident upon the rear surface of the second electrodes 3a,3b which are preferably spaced away from the central axis. In this mode of operation the ion 10 beam transmission through the exit slit or electrode 5 is preferably zero or substantially zero.

Fig. 5 shows a subsequent high transmission mode of operation wherein at a second later time T2 the first electrodes 2a,2b, second electrodes 3a,3b and third 15 electrodes 4a,4b are held at potentials (e.g. the same potential) such that the ion beam is now fully transmitted through the exit slit or electrode 5.

According to the preferred embodiment the ion beam attenuator (e.g. Einzel lens arrangement or less 20 preferably another form of ion beam attenuator) is preferably repeatedly switched back and forth between a high transmission mode of operation and a low transmission mode of operation. According to less preferred embodiments the ion beam attenuator may also 25 be switched to one or more further or intermediate modes. The degree of attenuation of the ion beam depends upon the relative amounts of time the ion beam attenuator spends in the high and low transmission modes.

30 According to the preferred embodiment the ion beam is mass analysed on a much slower timescale than the speed of switching the ion beam attenuator between modes. For example, with a conventional arrangement the

Einzel lens is switched to a low transmission mode of operation and then the ion beam is mass analysed. The Einzel lens is then switched to a high transmission mode of operation and the ion beam is then again mass

5 analysed again. Accordingly, the mass analyser acquires, samples or mass analyses an ion beam at the same rate and in a synchronous manner to the switching of the Einzel lens. In contrast, according to the preferred embodiment it is the repeated switching

10 between modes of the ion beam attenuator which reduces the intensity of the ion beam and the switching between modes may be faster and asynchronous to the acquisition rate of the mass analyser. For example, according to an embodiment the ion beam attenuator may be switched, for

15 example, at least 50-100 times between different modes to reduce the intensity of the ion beam before the ion beam is mass analysed i.e. the acquisition rate of the mass analyser may be much slower than the speed of switching the ion beam attenuator. Furthermore, the

20 rate of acquisition of the mass analyser is preferably essentially asynchronous to and decoupled from the switching of the ion beam attenuator.

Fig. 6 shows a voltage timing diagram according to a preferred embodiment wherein a gate or retarding

25 voltage is applied to or switched ON to the third electrodes 4a,4b (or is otherwise switched ON) starting at a time T1 and lasting for a time period $\Delta T1$. During the time period $\Delta T1$ the transmission of the ion beam 1 through the exit slit or electrode 5 remains

30 substantially zero i.e. ions are reflected away from the third electrodes 4a,4b back towards the rear surface of the second electrodes 3a,3b whereupon they impinge. Substantially no ions therefore exit the ion beam

attenuator in this mode of operation. At the end of the time period ΔT_1 the gate or retarding voltage applied to the third electrodes 4a,4b is then preferably switched OFF. The gate or retarding voltage then preferably 5 remains OFF for a time period ΔT_2 which is preferably shorter than the time period ΔT_1 . During the time period ΔT_2 during which the gate or retarding voltage remains switched OFF the transmission of the ion beam through the exit slit or electrode 5 is preferably high 10 and may be substantially 100%.

The cycle of switching a gate or regarding voltage ON for a time period ΔT_1 and then switching the gate or retarding voltage OFF for a subsequent time period ΔT_2 is preferably repeated multiple times in preferably a 15 regular manner as illustrated in Fig. 6. For example, the ion beam attenuator may be switched at a rate which is preferably 50-100 times faster than the acquisition rate of a mass analyser used to mass analyse the ion beam. According to less preferred embodiments the ion 20 beam attenuator may be switched between modes in a non-regular or variable manner.

The preferred electrode arrangement as operated according to the preferred embodiment can be considered to comprise a pulsed transmission ion gate or ion beam 25 attenuator having a mark space ratio given by:

$$\Delta T_2 / \Delta T_1$$

The average relative transmission of the ion beam 30 will be proportional to the duty cycle of the ion gate which is given by:

$\Delta T_2 / (\Delta T_1 + \Delta T_2)$

In the voltage timing diagram shown in Fig. 6 the mark space ratio $\Delta T_2 / \Delta T_1$ is 1:9 and the duty cycle is 5 0.1. Therefore, the ion beam intensity is attenuated by the ion beam attenuator by 90% i.e. the ion beam exiting the ion beam attenuator is only 10% of the intensity of the ion beam received by the ion beam attenuator.

Fig. 7 shows an alternative low transmission mode 10 of operation wherein the ion beam is deflected (rather than reflected) by the application of a raised positive voltage to one of the second electrodes 3a. The ion beam attenuator may therefore be considered in this embodiment to comprise a pulsed transmission ion gate 15 having a deflection electrode 3a. During the time period ΔT_1 of zero ion transmission a deflection voltage is preferably applied to the deflection electrode 3a such that the ion beam passing through the ion beam attenuator is deflected and falls incident upon the 20 front surface of one of the third electrodes 4b. As a result the ion transmission through the exit slit or electrode 5 is preferably substantially zero. The ion beam attenuator is then preferably switched to a high transmission mode of operation wherein the deflection 25 voltage applied to one of the second electrodes 3a is preferably turned OFF (or substantially reduced) for a time period ΔT_2 . Accordingly, the transmission of the ion beam through the exit slit or electrode 5 is correspondingly high in this mode of operation. The 30 time period ΔT_2 is preferably shorter than the time period ΔT_1 .

The ion beam 1b which emerges from the preferred ion beam attenuator 6 preferably has an overall average intensity which is lower than the intensity of the ion beam 1a received by the ion beam attenuator 6 i.e. the 5 number of ions emerging per unit time is reduced. In a preferred embodiment the total cycle time (i.e. the sum of the time period ΔT_1 spent in a low or zero transmission mode of operation and the time period ΔT_2 spent in a high transmission mode) of the ion beam 10 attenuator 6 is preferably of the order of 100-1000 μs . However, according to less preferred embodiments the 15 total cycle time may be shorter or longer than this.

According to the preferred embodiment the degree of attenuation of an ion beam by the ion beam attenuator 6 20 is controlled by controlling the duty cycle of the ion beam attenuator 6. For example, in order to increase the degree or amount of attenuation of the ion beam the mark space ratio or duty cycle may be varied such that the time period ΔT_1 spent in a low or zero transmission mode of operation is relatively increased compared to 25 the time period ΔT_2 spent in a high transmission mode of operation.

According to an embodiment one or more ion guides 30 may be arranged upstream and/or downstream of the ion beam attenuator 6. At least one of the ion guides may be maintained at a pressure in the range $> 10^{-3}$ mbar and may preferably act as a gas collision cell. The relatively high pressure ion guide may be arranged so as to effectively decouple the ion beam attenuator 6 from the rest of the mass spectrometer. According to an 35 embodiment the high pressure ion guide or gas cell may be arranged downstream of the ion beam attenuator. The

relatively high pressure ion guide preferably improves operation of the mass spectrometer when the ion beam attenuator 6 is used in conjunction with an orthogonal acceleration Time of Flight (TOF) mass analyser.

5 The ion guide may comprise an AC or RF multipole rod set, a segmented RF or AC multipole rod set, an AC or RF stacked ring ion tunnel ion guide or an AC or RF stacked ring ion funnel ion guide. The ion guide may optionally utilise a linear acceleration field (i.e. a
10 constant DC voltage gradient) and/or a traveling DC voltage or voltage waveform may be applied to the electrodes of the ion guide in order to propel ions through or along at least a portion of the ion guide.
The traveling DC voltage method preferably involves
15 applying one or more time varying or transient DC potentials or DC potential waveforms to at least a portion of the one or more ion guides in order to urge ions along at least a portion of the one or more ion guides. This approach may also be used to ensure that
20 ions are resident in the ion guide for a total time applicable to the particular mode of operation of the pulsed ion gate.

Advantageously, an ion beam can preferably be attenuated by a precisely controlled amount using the
25 preferred ion beam attenuator 6 without affecting the mass resolution, mass calibration or mass accuracy of, for example, an orthogonal acceleration Time of Flight mass analyser or other form of mass analyser arranged downstream of the ion beam attenuator and optional ion guide.

A particularly preferred embodiment is contemplated comprising either an Electrospray or MALDI ion source, followed by an ion guide. The ion guide is followed by

a first mass filter preferably a quadrupole rod set mass filter. An ion beam attenuator according to a preferred embodiment is then preferably arranged downstream of the first mass filter. A gas cell or relatively high pressure ion guide may be arranged downstream of the ion beam attenuator. A Time of Flight mass analyser or other form of mass analyser is preferably arranged downstream of the gas cell and ion beam attenuator. Such an arrangement allows MS and MS-MS experiments to be performed.

Fig. 8 shows a SIMION (RTM) model of an ion beam attenuator 6 according to a preferred embodiment in a high transmission mode of operation. In this mode of operation the ion beam attenuator 6 was arranged to transmit ions with preferably 100% efficiency. Fig. 8 shows the path taken by a beam of positive ions 1a having an axial energy of 3eV and exiting an RF-only hexapole ion guide 10 maintained at a relatively low pressure arranged upstream of the ion beam attenuator 6. The hexapole ion guide 10 was maintained at a relative potential of 0V. The first electrodes 2a,2b of the ion beam attenuator 6 were held at a relative potential of -57V, the second electrodes 3a,3b were held at a relative potential of -2V and the third electrodes 4a,4b were held at a relative potential of -1V. A relatively high pressure ion guide 8 was modelled as being provided downstream of the ion beam attenuator 6 to receive ions emitted by the ion beam attenuator 6. The ion guide 8 was modelled as being held at a relative potential of -2V. As can be seen from Fig. 8 ions were focussed by the ion beam attenuator 6 to a point just beyond or downstream of the second electrodes 3a,3b and between the second electrodes 3a,3b and the third electrodes

4a,4b. The ions are shown onwardly transmitted to the ion guide 8 with a high (e.g. 100%) transmission.

Fig. 9 shows a three-dimensional potential energy diagram showing the potential energy profile within the 5 ion beam attenuator 6 when the ion beam attenuator 6 is maintained in the high transmission mode as described above in relation to Fig. 8.

Fig. 10 shows a SIMION (RTM) model of an ion beam attenuator 6 according to a preferred embodiment in a 10 low transmission mode of operation. In this mode of operation the ion beam attenuator 6 was arranged to substantially attenuate ions, preferably such that no ions exit the ion beam attenuator 6 in this mode of operation. Fig. 10 shows the ion path taken by a beam 15 of positive ions 1a having an axial energy of 3eV and exiting an RF-only hexapole ion guide 10 maintained at a relatively low pressure. The hexapole ion guide 10 was maintained at a relative potential of 0V. One of the first electrodes 2a was held at a relative potential of 20 -47V and the other of the first electrodes 2b was held at a relative potential of -67V. The second electrodes 3a,3b were both held at a relative potential of +8V and the third electrodes 4a,4b were both held at a relative potential of -1V. As with the embodiment shown and 25 described in relation to Figs. 8 and 9, a relatively high pressure ion guide 8 is shown located downstream of the ion beam attenuator 6 and was modelled as being held at a relative potential of -2V. Ions were accelerated by the first electrodes 2a,2b but they were also 30 deflected off axis by the different potentials at which the first electrodes 2a,2b were maintained. The ions were then retarded by the relatively high potentials at which the second electrodes 3a,3b were maintained (e.g.

+8V). Ions which were retarded by the electric field between the first electrodes 2a,2b and the second electrodes 3a,3b were reaccelerated back towards the rear surface of one of the first electrodes 2a.

- 5 Preferably, none of the ions pass beyond the second electrodes 3a,3b and hence preferably no ions exit the ion beam attenuator 6 in this mode of operation. The ion transmission through the ion beam attenuator 6 is therefore preferably zero in this low transmission mode
10 of operation.

Fig. 11 shows a three-dimensional potential energy diagram showing the potential energy profile within the ion beam attenuator 6 when the ion beam attenuator 6 is maintained in the low transmission mode as described
15 above in relation to Fig. 10.

Fig. 12 shows an experimentally determined relationship between the observed relative transmission of an ion beam through the preferred ion beam attenuator 6 and the duty cycle of the ion beam attenuator 6
20 according to the preferred embodiment. It can be seen that there is a direct and predictable relationship between the relative transmission and the duty cycle of the ion beam attenuator 6. For clarity the data shown in Fig. 12 has been re-plotted in Fig. 13 as log of the
25 relative transmission versus log of the duty cycle of the ion beam attenuator. The cycle time for the particular experiment, the results of which are shown in both Figs. 12 and 13, was fixed at 300 μ s.

Fig. 14A shows a mass spectrum obtained using an
30 Electrospray Ionisation ion source and MS-MS analysis with an orthogonal acceleration Time of Flight mass spectrometer incorporating a preferred ion beam attenuator. The mass spectrum was obtained by infusing

(Glu)-fibrinopeptide-B (having a mass to charge ratio of 785.8). The mass spectrum shown in Fig. 14A was acquired when the ion beam attenuator was constantly operated at full transmission i.e. was effectively
5 redundant. Ten mass spectra were obtained, each over a period of 1.2 s. The ten mass spectra were then averaged to produce the mass spectrum shown in Fig. 14A.

Fig. 14B shows a mass spectrum obtained in a similar manner to that shown in Fig. 14A except that
10 the ion beam was attenuated by 90% by an ion beam attenuator operated according to the preferred embodiment. The ion beam attenuator 6 was pulsed with a duty cycle of 0.1 and a total cycle time of 300 μ s. 100 mass spectra were obtained, each over a period of 1.2 s.
15 The 100 mass spectra were then averaged to produce the mass spectrum shown in Fig. 14B. It can be seen from comparing Figs. 14A and 14B that the amount of attenuation is constant for peaks over the entire mass range shown i.e. the ion beam attenuator advantageously
20 attenuates the ion beam independently of the mass to charge ratio of ions in the ion beam. The precise measured attenuation factor based upon the intensity of the most intense peak having a mass to charge ratio of 684.35 was determined to be 89.9%.

25 Fig. 15A shows in greater detail the mass spectrum shown in Fig. 14A across the narrower mass range m/z 1171 to 1175. Similarly, Fig. 15B shows in greater detail the mass spectrum shown in Fig. 14B across the narrower mass range m/z 1171 to 1175. No effect on peak
30 resolution peak shape or mass to charge ratio is evident due to the action of the ion beam attenuator.

The preferred ion beam attenuator described above may be used, for example, to provide controlled

attenuation of a continuous ion beam which is then subsequently mass analysed by an orthogonal acceleration Time of Flight mass analyser, an axial acceleration Time of Flight mass analyser, a 3D ion trap mass analyser, a 5 2D linear ion trap mass analyser, a Fourier Transform Ion Cyclotron Resonance ("FTICR") mass analyser, a magnetic sector mass analyser or a quadrupole mass analyser.

Embodiments are contemplated wherein an ion beam 10 passing through the ion beam attenuator may be subjected to MS, MSMS or MSⁿ analysis.

The preferred ion beam attenuator as described above may be used, for example, to provide controlled attenuation of an ion beam emitted from an ion source 15 such as, for example, an Electrospray Ionisation ion source, an APPI ion source, an APCI ion source, a Matrix Assisted Laser Desorption Ionisation ion source, a LDI ion source, an APMALDI ion source, a DIOS ion source, an Electron Impact ion source, a CI ion source, a FI ion 20 source, a FD ion source, an ICP ion source, a FAB ion source or a LSIMS ion source.

According to an embodiment of the present invention the attenuation factor of ion beam attenuator may be automatically and precisely controlled during analysis. 25 For example, a measurement of the ion current may be made at regular intervals during an analysis. The amount of attenuation required may then be repeatedly calculated from this measurement as the analysis proceeds. The measurement of ion current may be made, 30 for example, by examination of the mass spectral data recorded as the analysis proceeds. The total ion current recorded or the ion current at one or more selected mass to charge ratios may then be used to

determine the attenuation factor of the ion beam attenuator for the next mass spectrum to be recorded.

According to another embodiment during the period of time that the ion beam attenuator is operated in a zero transmission mode of operation, ions may be directed towards a separate ion detector preferably close to the ion beam attenuator. The signal recorded using this ion detector may be used to calculate the total ion current at the ion beam attenuator based on the duty cycle. This measurement may then be used to calculate a new duty cycle for the ion gate or ion beam attenuator if the ion current exceeds the allowable level which can be accommodated by the mass analyser or ion detector employed. For example, this method provides a way of automatically reducing the number of ions per unit time which enter an ion trap mass analyser based upon the known maximum number of ions which can be permitted.

According to other less preferred embodiments the ion beam may be rapidly pulsed between zero (or low) transmission and a relatively high transmission using other electrostatic, magnetic or mechanical arrangements. For example, according to a less preferred embodiment a mechanical shutter may be used as an ion beam attenuator.

According to a less preferred embodiment the transmission does not necessarily have to be reduced to zero during the low transmission mode. Instead, for example, the transmission may be reduced to a transmission > 0%. However, if the ion transmission in the low transmission mode of operation is not reduced to 0% then there may be a risk of surface charging effects

occurring which could cause instability in the attenuation factor by which the ion beam is attenuated.

- Although the present invention has been described with reference to preferred embodiments, it will be
5 understood by those skilled in the art that various changes in form and detail may be made without departing from the scope of the invention as set forth in the accompanying claims.

Claims

- 5 1. A mass spectrometer comprising:
 an ion beam attenuator for attenuating a beam of
 ions, wherein, in use, the beam of ions has a first
 intensity prior to passing through said ion beam
 attenuator and has a second intensity downstream of said
10 ion beam attenuator, wherein said second intensity is x%
 of said first intensity;
 wherein, in use, said ion beam attenuator
 attenuates said beam of ions from said first intensity
 to said second intensity by being repeatedly switched
15 between a low transmission mode of operation wherein the
 transmission of ions through the ion beam attenuator is
 substantially y% and a high transmission mode of
 operation wherein the transmission of ions through the
 ion beam attenuator is z%, wherein z>y.
20
2. A mass spectrometer as claimed in claim 1, wherein
 x is selected from the group consisting of: (i) < 0.1;
 (ii) 0.1-0.5; (iii) 0.5-1; (iv) 1-5; (v) 5-10; (vi) 10-
 15; (vii) 15-20; (viii) 20-25; (ix) 25-30; (x) 30-35;
25 (xi) 35-40; (xii) 40-45; (xiii) 45-50; (xiv) 50-55; (xv)
 55-60; (xvi) 60-65; (xvii) 65-70; (xviii) 70-75; (xix)
 75-80; (xx) 80-85; (xxi) 85-90; (xxii) 90-95; and
 (xxiii) 95-99.99.
30 3. A mass spectrometer as claimed in claim 1 or 2,
 wherein y = 0.

4. A mass spectrometer as claimed in claim 1 or 2, wherein $y > 0$.

5. A mass spectrometer as claimed in claim 4, wherein
y is selected from the group consisting of: (i) < 0.1 ;
(ii) 0.1-0.5; (iii) 0.5-1; (iv) 1-5; (v) 5-10; (vi) 10-
15; (vii) 15-20; (viii) 20-25; (ix) 25-30; (x) 30-35;
(xi) 35-40; (xii) 40-45; (xiii) 45-50; (xiv) 50-55; (xv)
55-60; (xvi) 60-65; (xvii) 65-70; (xviii) 70-75; (xix)
10 75-80; (xx) 80-85; (xxi) 85-90; and (xxii) > 90 .

6. A mass spectrometer as claimed in any preceding
claim, wherein $z = 100$.

15 7. A mass spectrometer as claimed in any of claims 1-
5, wherein $z < 100$.

8. A mass spectrometer as claimed in claim 7, wherein
z is selected from the group consisting of: (i) < 1 ;
20 (ii) 1-5; (iii) 5-10; (iv) 10-15; (v) 15-20; (vi) 20-25;
(vii) 25-30; (viii) 30-35; (ix) 35-40; (x) 40-45; (xi)
45-50; (xii) 50-55; (xiii) 55-60; (xiv) 60-65; (xv) 65-
70; (xvi) 70-75; (xvii) 75-80; (xviii) 80-85; (xix) 85-
90; (xx) 90-95; and (xxi) 95-99.99.

25

9. A mass spectrometer as claimed in any preceding
claim, wherein said ion beam attenuator is in said low
transmission mode of operation for a time period ΔT_1 and
is in said high transmission mode of operation for a
30 time period ΔT_2 .

10. A mass spectrometer as claimed in claim 9, wherein
 $\Delta T_1 > \Delta T_2$.

11. A mass spectrometer as claimed in claim 9 or 10,
wherein said time period ΔT_1 is selected from the group
consisting of: (i) < 0.1 μ s; (ii) 0.1-0.5 μ s; (iii) 0.5-
5 1 μ s; (iv) 1-50 μ s; (v) 50-100 μ s; (vi) 100-150 μ s;
(vii) 150-200 μ s; (viii) 200-250 μ s; (ix) 250-300 μ s;
(x) 300-350 μ s; (xi) 350-400 μ s; (xii) 450-500 μ s;
(xiii) 500-550 μ s; (xiv) 550-600; (xv) 600-650 μ s; (xvi)
10 650-700 μ s; (xvii) 700-750 μ s; (xviii) 750-800 μ s; (xix)
800-850 μ s; (xx) 850-900 μ s; (xxi) 900-950 μ s; (xxii)
950-1000 μ s; (xxiii) 1-10 ms; (xxiv) 10-50 ms; (xxv) 50-
100 ms; (xxvi) > 100 ms.
12. A mass spectrometer as claimed in claim 9, 10 or
15 11, wherein said time-period ΔT_2 is selected from the
group consisting of: (i) < 0.1 μ s; (ii) 0.1-0.5 μ s;
(iii) 0.5-1 μ s; (iv) 1-50 μ s; (v) 50-100 μ s; (vi) 100-
150 μ s; (vii) 150-200 μ s; (viii) 200-250 μ s; (ix) 250-
300 μ s; (x) 300-350 μ s; (xi) 350-400 μ s; (xii) 450-500
20 μ s; (xiii) 500-550 μ s; (xiv) 550-600; (xv) 600-650 μ s;
(xvi) 650-700 μ s; (xvii) 700-750 μ s; (xviii) 750-800 μ s;
(xix) 800-850 μ s; (xx) 850-900 μ s; (xxi) 900-950 μ s;
(xxii) 950-1000 μ s; (xxiii) 1-10 ms; (xxiv) 10-50 ms;
25 (xxv) 50-100 ms; (xxvi) > 100 ms.
13. A mass spectrometer as claimed in any of claims 9-
12, further comprising a control device wherein, in use,
said control device adjusts either the time period ΔT_1
and/or the time period ΔT_2 in order to adjust said
30 second intensity.
14. A mass spectrometer as claimed in any of claims 9-
13, wherein in use the mark space ratio $\Delta T_2/\Delta T_1$ is

adjusted in order to adjust the ratio of said second intensity to said first intensity.

15. A mass spectrometer as claimed in any of claims 9-
5 14, further comprising an ion detector wherein in said low transmission mode of operation at least a portion of the beam of ions is substantially directed towards said ion detector and wherein said ion detector measures the ion current of said beam of ions.
10
16. A mass spectrometer as claimed in claim 15, wherein said control device adjusts either the time period ΔT_1 and/or the time period ΔT_2 in order to adjust said second intensity based upon the ion current as measured
15 by said ion detector.
17. A mass spectrometer as claimed in any preceding claim, wherein said ion beam attenuator is in said low transmission mode of operation for a time period ΔT_1 and
20 is in said high transmission mode of operation for a time period ΔT_2 and wherein in the event of one or more mass peaks in one or more mass spectra being determined to suffer from saturation effects or approaching saturation then either the time period ΔT_1 and/or the
25 time period ΔT_2 are adjusted in order to adjust said second intensity.
18. A mass spectrometer as claimed in any preceding claim, wherein said ion beam attenuator is in said low
30 transmission mode of operation for a time period ΔT_1 and is in said high transmission mode of operation for a time period ΔT_2 and wherein in the event of mass data or mass spectral data being determined to suffer from

saturation effects or approaching saturation then either the time period ΔT_1 and/or the time period ΔT_2 are adjusted in order to adjust said second intensity.

- 5 19. A mass spectrometer as claimed in any preceding claim, wherein said ion beam attenuator is in said low transmission mode of operation for a time period ΔT_1 and is in said high transmission mode of operation for a time period ΔT_2 and wherein in the event of the ion current being determined to exceed a certain level then either the time period ΔT_1 and/or the time period ΔT_2 are adjusted in order to adjust said second intensity.
- 10
- 15 20. A mass spectrometer as claimed in any preceding claim, wherein said ion beam attenuator comprises an electrostatic lens.
- 20
- 25 21. A mass spectrometer as claimed in claim 20, wherein said electrostatic lens comprises a plurality of electrodes wherein first voltages are applied to at least some of said electrodes in said low transmission mode of operation and wherein second different voltages are applied to at least some of said electrodes in said high transmission mode of operation.
- 25
- 30 22. A mass spectrometer as claimed in claim 20 or 21, wherein said electrostatic lens comprises an Einzel lens comprising at least three electrodes.
- 30 23. A mass spectrometer as claimed in any preceding claim, wherein in said low transmission mode of operation said beam of ions is: (a) retarded or reflected; and/or (b) deflected or diverted.

24. A mass spectrometer as claimed in any preceding claim, wherein said ion beam attenuator comprises a mechanical shutter.

5

25. A mass spectrometer as claimed in any preceding claim, wherein said ion beam attenuator comprises a magnetic ion gate.

10 26. A mass spectrometer as claimed in any preceding claim, further comprising one or more mass filters arranged upstream and/or downstream of said ion beam attenuator.

15 27. A mass spectrometer as claimed in any preceding claim, further comprising one or more ion guides arranged upstream and/or downstream of said ion beam attenuator.

20 28. A mass spectrometer as claimed in claim 27, wherein said one or more ion guides are maintained, in use, at a pressure selected from the group consisting of: (i) < 0.001 mbar; (ii) 0.001-0.005 mbar; (iii) 0.005-0.01 mbar; (iv) 0.01-0.05 mbar; (v) 0.05-0.1 mbar; (vi) 0.1-
25 0.5 mbar; (vii) 0.5-1 mbar; and (viii) > 1 mbar.

29. A mass spectrometer as claimed in claim 27 or 28, wherein said one or more ion guides comprise a gas collision cell.

30

30. A mass spectrometer as claimed in claim 27, 28 or 29, wherein in use one or more axial DC potential gradients are maintained along at least 5%, 10%, 15%,

20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%,
75%, 80%, 85%, 90%, 95% or 100% of said one or more ion
guides.

5 31. A mass spectrometer as claimed in any of claims 27-
30, wherein in use one or more time varying DC
potentials or DC potential waveforms are applied to at
least a portion of said one or more ion guides so that
at least some ions are urged along said one or more ion
10 guides.

32. A mass spectrometer as claimed in any of claims 27-
31, wherein in use one or more axial trapping regions
are provided within said one or more ion guides and
15 wherein said one or more axial trapping regions are
translated along at least a portion of said one or more
ion guides.

33. A mass spectrometer as claimed in any of claims 27-
20 32, wherein said one or more ion guides are selected
from the group consisting of: (i) an RF or AC multipole
rod set ion guide; (ii) a segmented RF or AC multipole
rod set ion guide; (iii) an RF or AC ion tunnel ion
guide comprising a plurality of electrodes having
25 apertures through which ions are transmitted in use and
wherein at least 50% of said electrodes have
substantially similar sized apertures; and (iv) an RF or
AC ion funnel ion guide comprising a plurality of
electrodes having apertures through which ions are
30 transmitted in use and wherein at least 50% of said
electrodes have apertures which become progressively
larger or smaller.

34. A mass spectrometer as claimed in any preceding claim, further comprising a mass analyser.

35. A mass spectrometer as claimed in claim 34, wherein
5 said mass analyser acquires and mass analyses ions, in
use, with a frequency f_1 and wherein said ion beam
attenuator switches, in use, from said low transmission
mode of operation to said high transmission mode of
operation with a frequency f_2 .

10

36. A mass spectrometer as claimed in claim 35, wherein
frequency f_2 is asynchronous with frequency f_1 .

15 37. A mass spectrometer as claimed in claim 35 or 36,
wherein $f_2 > f_1$.

38. A mass spectrometer as claimed in claim 37, wherein
 f_2/f_1 is at least: (i) 2; (ii) 3; (iv) 4; (v) 5; (vi) 6;
(vii) 7; (viii) 8; (ix) 9; (x) 10; (xi) 15; (xii) 20;
20 (xiii) 25; (xiv) 30; (xv) 35; (xvi) 40; (xvii) 45;
(xviii) 50; (xix) 55; (xx) 60; (xxi) 65; (xxii) 70;
(xxiii) 75; (xxiv) 80; (xxv) 85; (xxvi) 90; (xxvii) 95;
(xxviii) 100; (xxix) 110; (xxx) 120; (xxxi) 130; (xxxii)
140; (xxxiv) 150; (xxxv) 160; (xxxvi) 170; (xxxvii) 180;
25 (xxxviii) 190; (xxxix) 200; (xxxx) 250; (xxxxi) 300;
(xxxxii) 350; (xxxxiii) 400; (xxxxiv) 450; and (xxxxv)
500.

39. A mass spectrometer as claimed in any of claims 34-
30 38, wherein said mass analyser is selected from the
group consisting of: (i) an orthogonal acceleration Time
of Flight mass analyser; (ii) an axial acceleration Time
of Flight mass analyser; (iii) a 3D ion trap mass

analyser; (iv) a linear ion trap mass analyser; (v) a Fourier Transform Ion Cyclotron Resonance mass analyser; (vi) a magnetic sector mass analyser; and (vii) a quadrupole mass analyser.

5

40. A mass spectrometer as claimed in any preceding claim, further comprising an ion source arranged upstream of said ion beam attenuator, wherein said ion source is selected from the group consisting of: (i) an 10 Electrospray ("ESI") ion source; (ii) an Atmospheric Pressure Photo Ionisation ("APPI") ion source; (iii) an Atmospheric Pressure Chemical Ionisation ("APCI") ion source; (iv) a Matrix Assisted Laser Desorption Ionisation ("MALDI") ion source; (v) a Laser Desorption 15 Ionisation ("LDI") ion source; (vi) an Atmospheric Pressure MALDI ("APMALDI") ion source; (vii) a Desorption-Ionisation on Silicon ("DIOS") ion source; (viii) an Electron Impact ("EI") ion source; (ix) a Chemical Ionisation ("CI") ion source; (x) a Field 20 Ionisation ("FI") ion source; (xi) a Field Desorption ("FD") ion source; (xii) an Inductively Coupled Plasma ("ICP") ion source; (xiii) a Fast Atom Bombardment ("FAB") ion source; (xiv) a Liquid Secondary Ions Mass Spectrometry ("LSIMS") ion source.

25

41. A mass spectrometer comprising:
an ion beam attenuator, wherein in use said ion beam attenuator attenuates an ion beam passing through an ion beam attenuator, wherein during one cycle said 30 ion beam attenuator substantially attenuates said ion beam for a time period ΔT_1 and substantially transmits said ion beam for a time period ΔT_2 ; and

a control device for adjusting the mark space ratio $\Delta T_2/\Delta T_1$ in order to adjust the degree of attenuation of said ion beam attenuator.

5 42. A mass spectrometer comprising:

an ion beam attenuator, wherein in use said ion beam attenuator attenuates an ion beam passing through an ion beam attenuator, wherein during one cycle said ion beam attenuator substantially attenuates said ion beam for a time period ΔT_1 and substantially transmits said ion beam for a time period ΔT_2 ;

a mass analyser for mass analysing ions transmitted by said ion beam attenuator; and

a control device for adjusting the mark space ratio $\Delta T_2/\Delta T_1$ in order to adjust the degree of attenuation of said ion beam attenuator and hence to adjust the intensity of an ion beam received by said mass analyser.

43. A method of mass spectrometry comprising:

20 passing a beam of ions having a first intensity to an ion beam attenuator;

attenuating said beam of ions by repeatedly switching said ion beam attenuator between a low transmission mode of operation wherein the transmission 25 of ions through the ion beam attenuator is substantially y% and a high transmission mode of operation wherein the transmission of ions through the ion beam attenuator is z%, wherein z>y; and

30 onwardly transmitting the beam of ions from said ion beam attenuator, wherein the beam of ions has a second intensity downstream of said ion beam attenuator, wherein said second intensity is x% of said first intensity.

44. A method of mass spectrometry comprising:

attenuating a continuous ion beam by an attenuation factor by passing said ion beam through an ion beam attenuator, wherein said ion beam attenuator is repeatedly switched between a low transmission mode of operation and a high transmission mode of operation, wherein said ion beam attenuator is in said low transmission mode of operation for a time period ΔT_1 and is in said high transmission mode of operation for a time period ΔT_2 ; and

adjusting either the time period ΔT_1 and/or the time period ΔT_2 in order to adjust said attenuation factor.

15

45. A method of mass spectrometry comprising:

transmitting a continuous ion beam having a first intensity to an ion beam attenuator;

repeatedly switching said ion beam attenuator between a low transmission mode of operation and a high transmission mode of operation, wherein said ion beam attenuator is in said low transmission mode of operation for a time period ΔT_1 and is in said high transmission mode of operation for a time period ΔT_2 ;

25 onwardly transmitting an ion beam having a second intensity from said ion beam attenuator, said second intensity being less than said first intensity;

determining whether said second intensity should be reduced; and

30 adjusting either the time period ΔT_1 and/or the time period ΔT_2 in order to reduce said second intensity.

46. A method of mass spectrometry comprising:

transmitting a continuous ion beam having a first intensity to an ion beam attenuator;

repeatedly switching said ion beam attenuator

5 between a low transmission mode of operation and a high transmission mode of operation, wherein said ion beam attenuator is in said low transmission mode of operation for a time period ΔT_1 and is in said high transmission mode of operation for a time period ΔT_2 ;

10 receiving ions exiting said ion beam attenuator in an ion guide, wherein the ions exiting said ion guide have a second intensity less than said first intensity;

determining whether said second intensity should be reduced; and

15 adjusting either the time period ΔT_1 and/or the time period ΔT_2 in order to reduce said second intensity.

47. A method of mass spectrometry comprising:

20 attenuating an ion beam by passing said ion beam through an ion beam attenuator, wherein during one cycle said ion beam attenuator substantially attenuates said ion beam for a time period ΔT_1 and substantially transmits said ion beam for a time period ΔT_2 ; and

25 adjusting the mark space ratio $\Delta T_2/\Delta T_1$ in order to adjust the degree of attenuation of said ion beam attenuator.

48. A method of mass spectrometry comprising:

30 attenuating an ion beam by passing said ion beam through an ion beam attenuator;

repeatedly switching the ion beam attenuator between a low transmission mode of operation and a high

transmission mode of operation with a relatively high frequency; and

mass analysing the ion beam transmitted by said ion beam attenuator with a mass analyser, wherein said mass analyser samples or acquires ions to be mass analysed with a relatively low frequency.

49. A method as claimed in claim 48, wherein the frequency of switching the ion beam attenuator between a low transmission mode of operation and a high transmission mode of operation is asynchronous with the frequency at which said mass analyser samples or acquires ions to be mass analysed.

15 50. A mass spectrometer comprising:

an ion beam attenuator for attenuating a beam of ions, wherein, in use, said ion beam attenuator is repeatedly switched between a low transmission mode of operation and a high transmission mode of operation; and

20 a mass analyser arranged to receive an attenuated beam of ions from said ion beam attenuator, wherein in use said mass analyser mass analyses said attenuated ion beam in an asynchronous manner to the switching between modes of said ion beam attenuator.

25

51. A mass spectrometer comprising:

an ion beam attenuator for attenuating a beam of ions, wherein, in use, said ion beam attenuator is repeatedly switched between a low transmission mode of operation and a high transmission mode of operation at a first frequency; and

a mass analyser arranged to received an attenuated beam of ions from said ion beam attenuator, wherein in

use said mass analyser mass analyses said attenuated ion beam with a second frequency, wherein said first frequency is greater than said second frequency.

5 52. A mass spectrometer as claimed in claim 51, wherein said first frequency is at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times greater than said second frequency.

10 53. A method of mass spectrometry comprising:
attenuating a beam of ions by repeatedly switching an ion beam attenuator between a low transmission mode of operation and a high transmission mode of operation; and

15 mass analysing an attenuated beam of ions emitted from said ion beam attenuator in an asynchronous manner to the switching between modes of said ion beam attenuator.

20 54. A method of mass spectrometry comprising:
attenuating a beam of ions by repeatedly switching at a first frequency an ion beam attenuator between a low transmission mode of operation and a high transmission mode of operation; and

25 mass analysing with a second frequency an attenuated beam of ions emitted from said ion beam attenuator, wherein said first frequency is greater than said second frequency.

30 55. A method of mass spectrometry as claimed in claim 54, wherein said first frequency is at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times greater than said second frequency.

56. A mass spectrometer comprising:
an ion beam attenuator;
a gas collision cell arranged downstream of said
5 ion beam attenuator; and
a mass analyser arranged downstream of said gas
collision cell;
wherein, in use, said ion beam attenuator is
switched between a high transmission mode of operation
10 and a low or zero transmission mode of operation at
least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 times
faster than said mass analyser samples or acquires ions
in order to mass analyse said ions.
- 15 57. A method of mass spectrometry comprising:
providing an ion beam attenuator, a gas collision
cell arranged downstream of said ion beam attenuator and
a mass analyser arranged downstream of said gas
collision cell; and
20 switching said ion beam attenuator between a high
transmission mode of operation and a low or zero
transmission mode of operation at least 10, 20, 30, 40,
50, 60, 70, 80, 90 or 100 times faster than said mass
analyser samples or acquires ions in order to mass
25 analyse said ions.
58. A mass spectrometer comprising:
an ion beam attenuator for attenuating an ion beam
by an attenuation factor wherein, in use, said ion beam
30 attenuator is repeatedly switched ON and OFF; and
a control device for varying the ratio of the time
that said ion beam attenuator is ON to the time that

said ion beam attenuator is OFF in order to vary said attenuation factor.

59. A method of mass spectrometry comprising:
5 attenuating an ion beam by an attenuation factor by repeatedly switching an ion beam attenuator ON and OFF; and
varying the ratio of the time that said ion beam attenuator is ON to the time that said ion beam attenuator is OFF in order to vary said attenuation factor.
- 10
60. A mass spectrometer comprising:
a device for repeatedly chopping an ion beam in
15 order to attenuate said ion beam.
61. A mass spectrometer as claimed in claim 60, wherein said device repeatedly reduces the transmission of said ion beam to 0%.
- 20
62. A method of mass spectrometry comprising:
repeatedly chopping an ion beam in order to attenuate said ion beam.
- 25
63. A method as claimed in claim 62, wherein said step of repeatedly chopping an ion beam comprises repeatedly reducing the transmission of said ion beam to 0%.
64. A mass spectrometer comprising:
30 a device for attenuating an ion beam wherein the degree of attenuation of said ion beam is determined by setting a mark space ratio of said device.

65. A method of mass spectrometry comprising:
setting a mark space ratio of an ion beam
attenuator in order to attenuate an ion beam by a
predetermined amount.

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

1/16

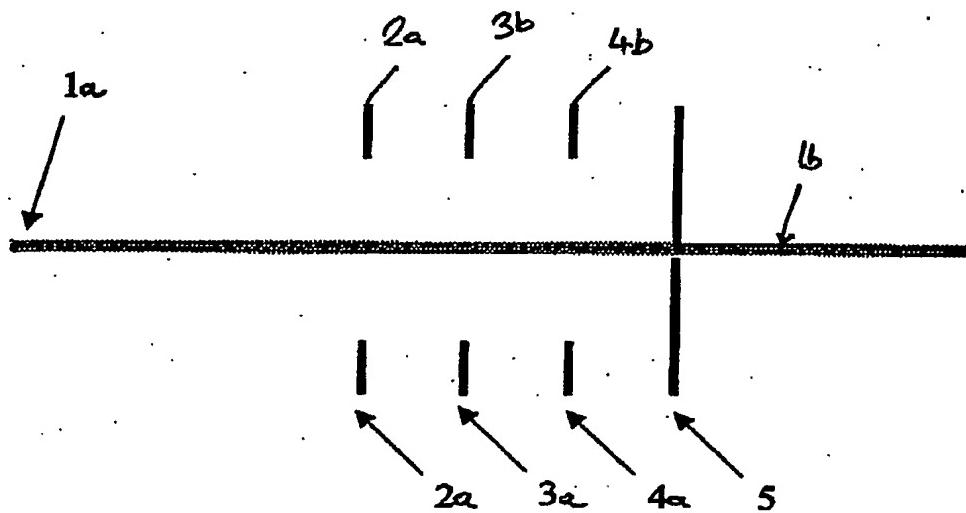


Figure 1

PRIOR ART

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

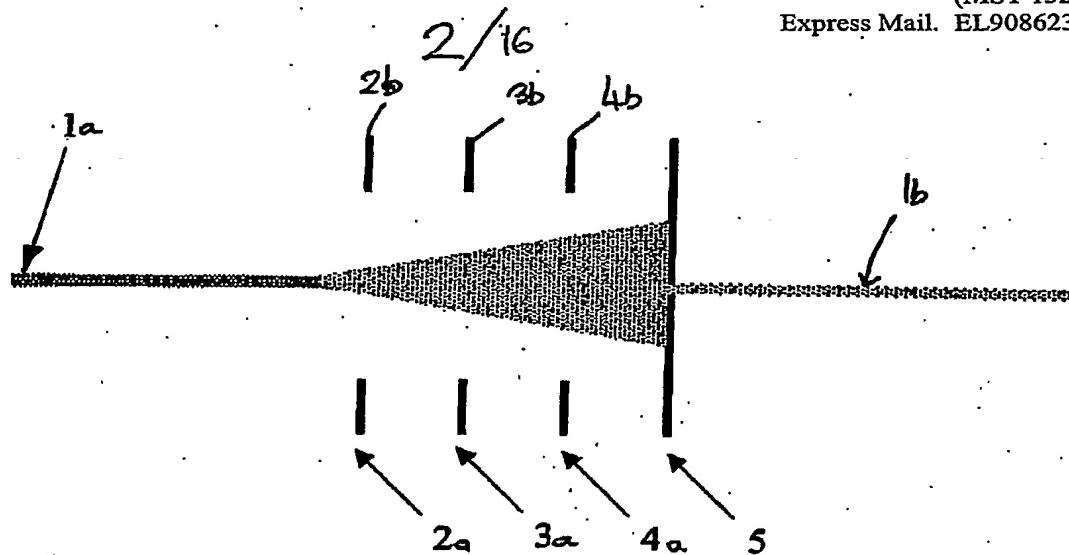


Figure 2

PRIOR ART

3/16

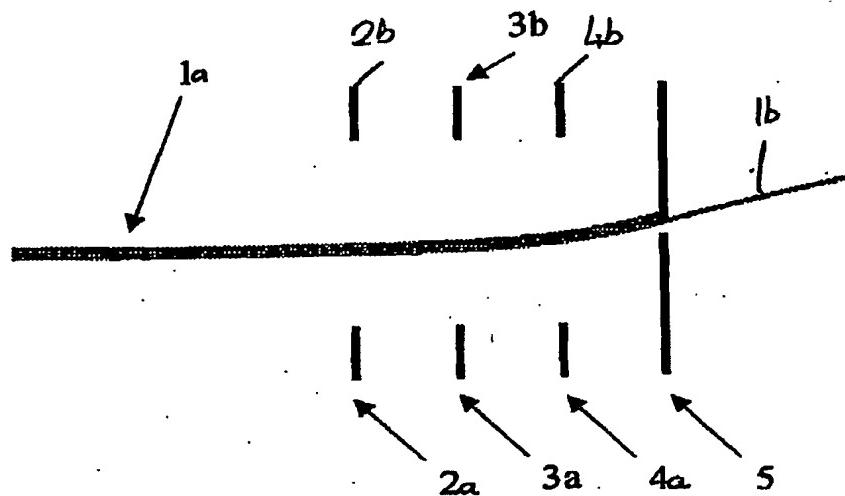


Figure 3

Prior Art

4/16

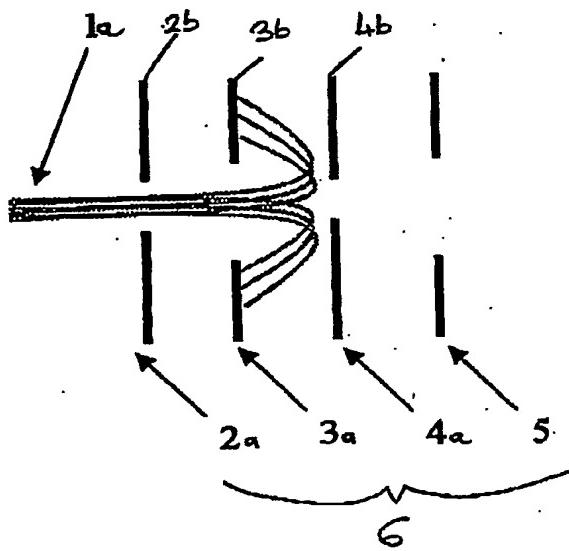


Figure 4

5 / 16

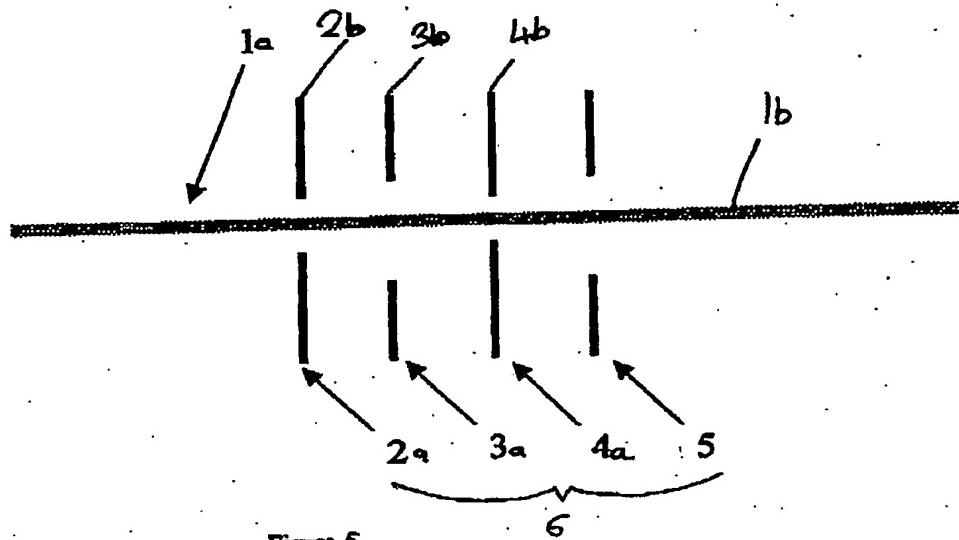


Figure 5

6/16

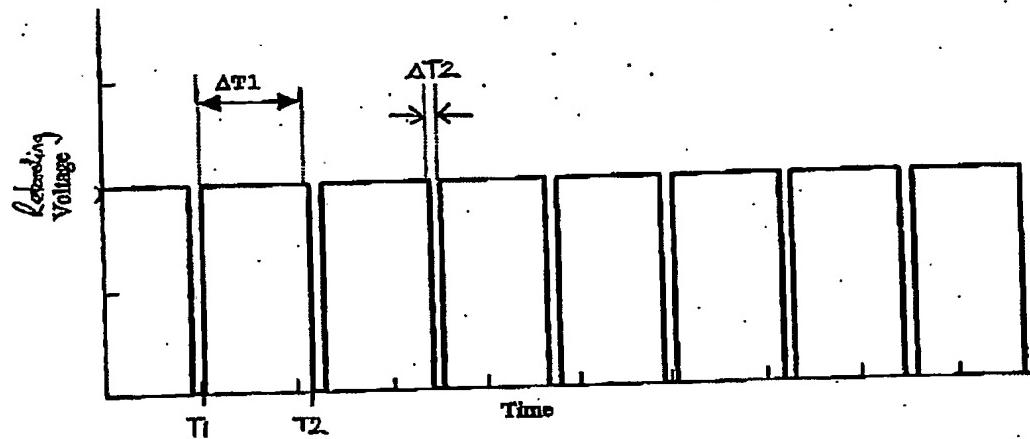
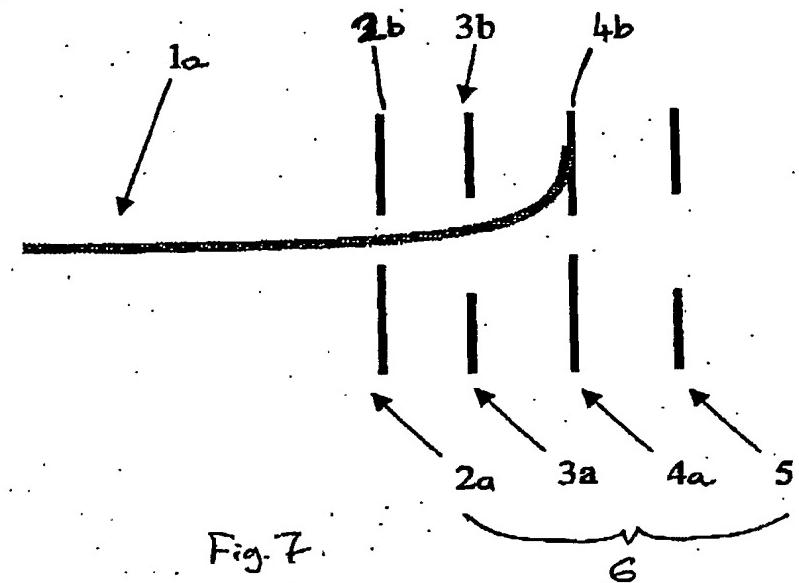


Fig. 6

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

7/16



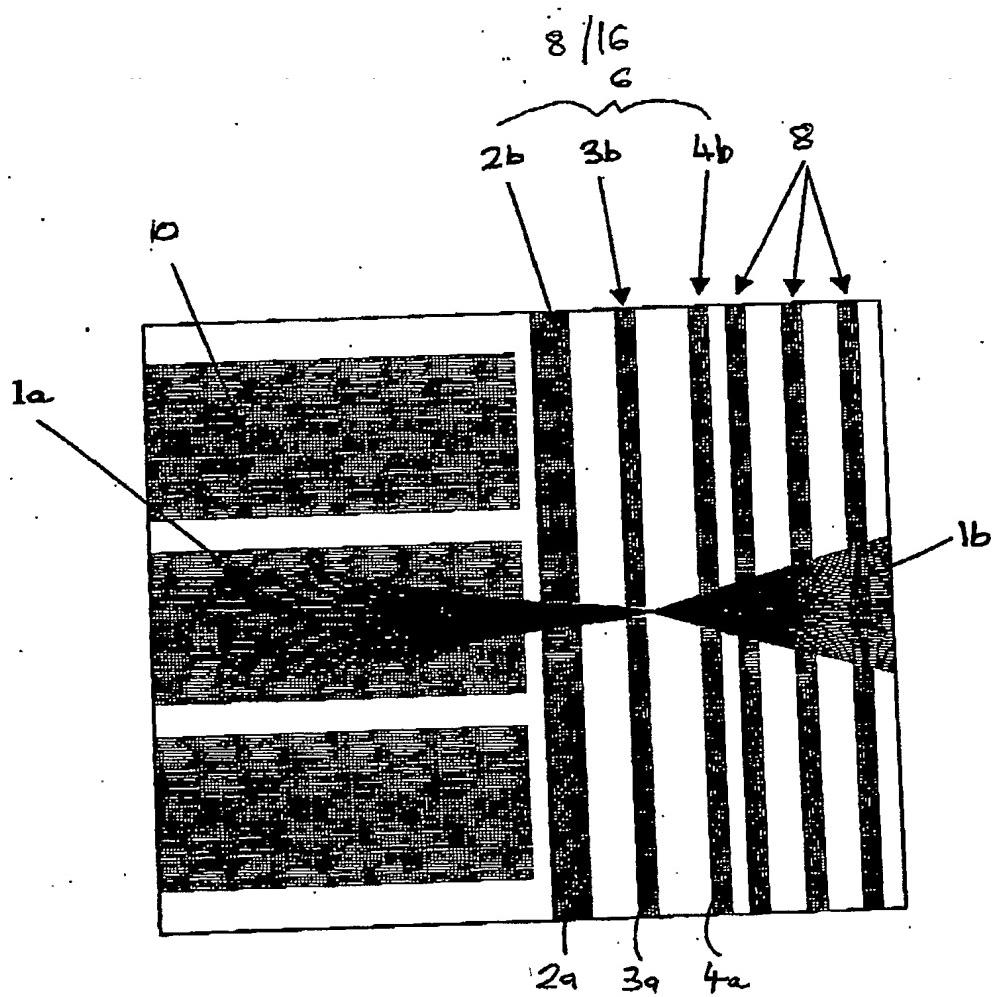


Fig. 8

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

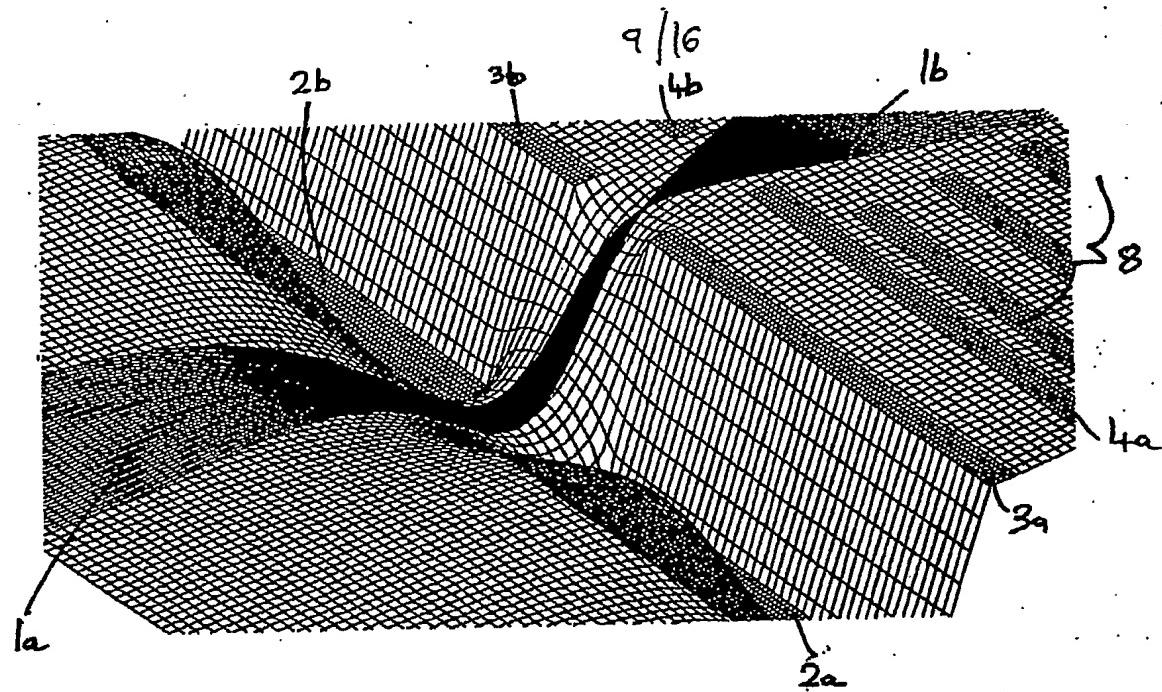


Fig. 9

10/16

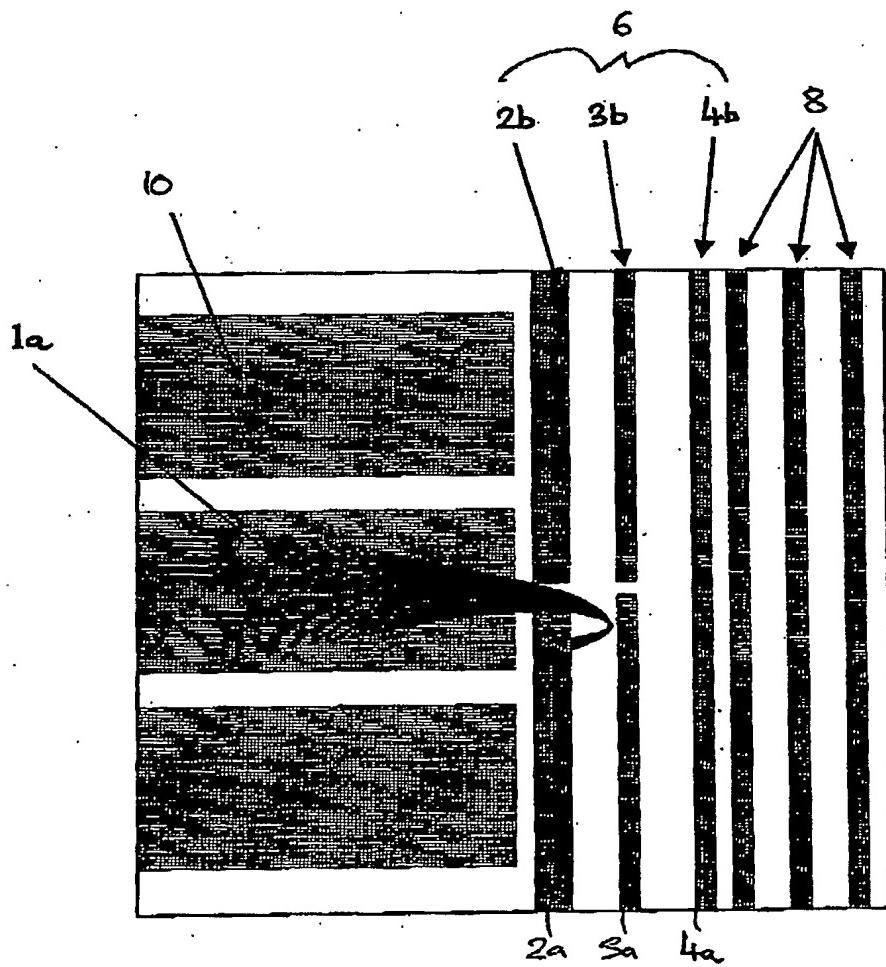


Fig. 10

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

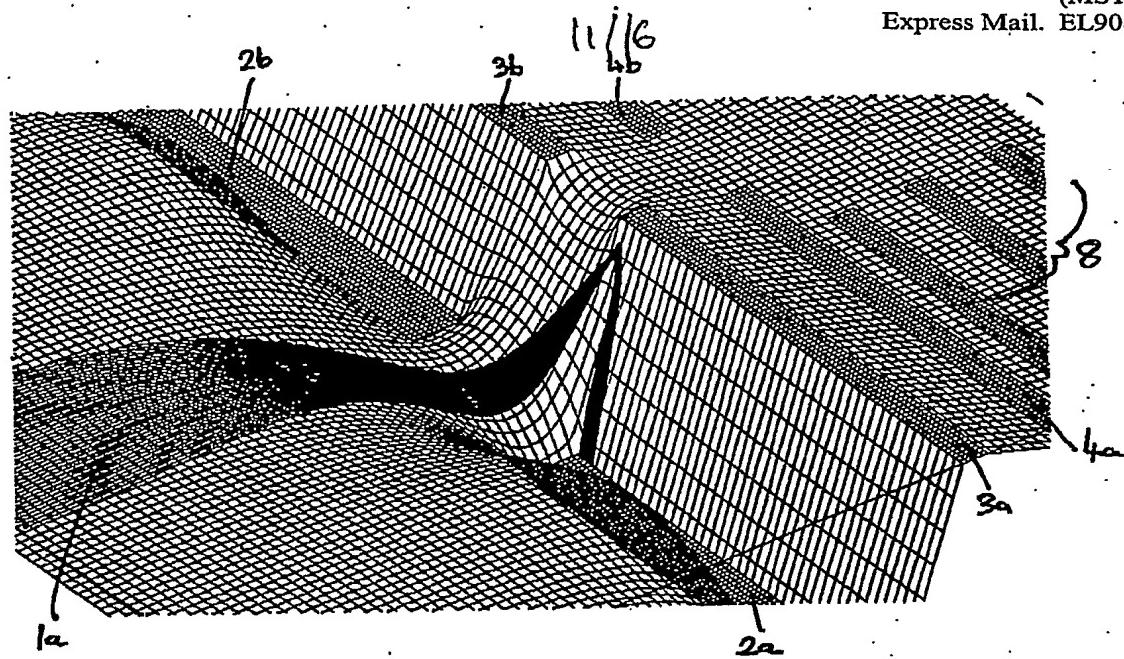


Fig. 11

12/16

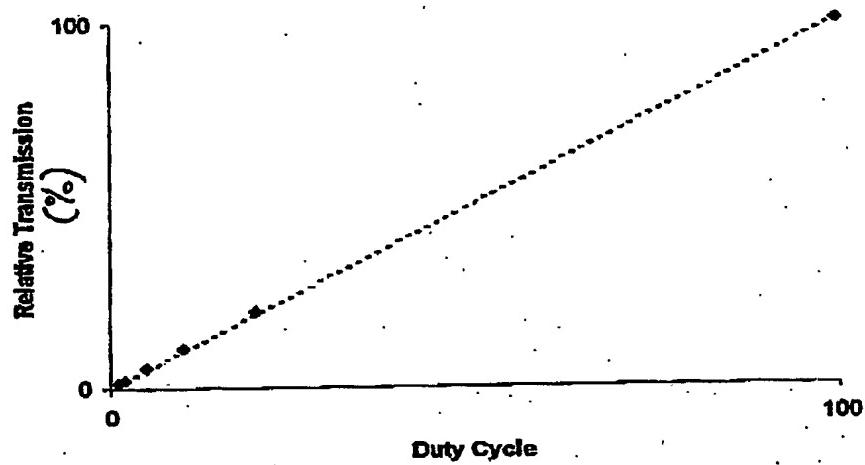


Fig. 12

13/16

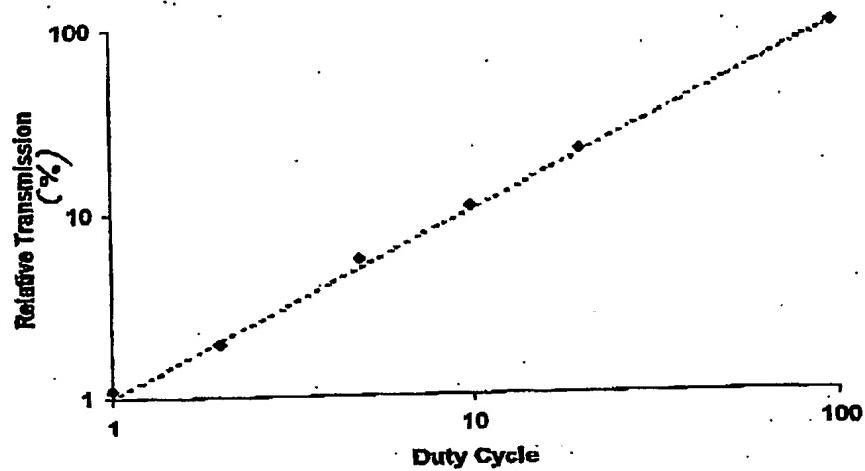


Fig. 13

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

14/16

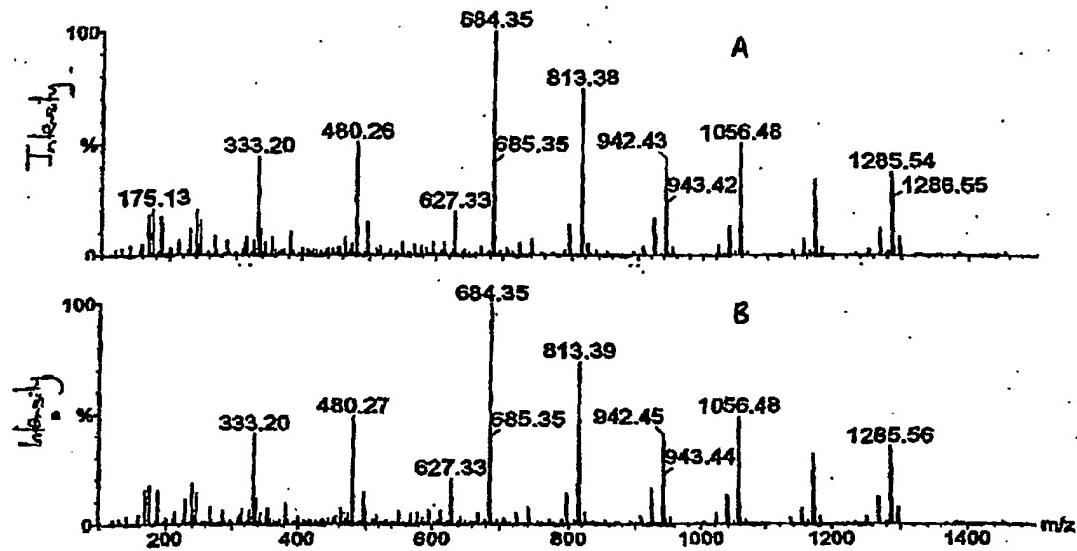


Fig. 14

Docket No. AE-MM-14
(MST 1329 US1)
Express Mail. EL908623385US

15/16

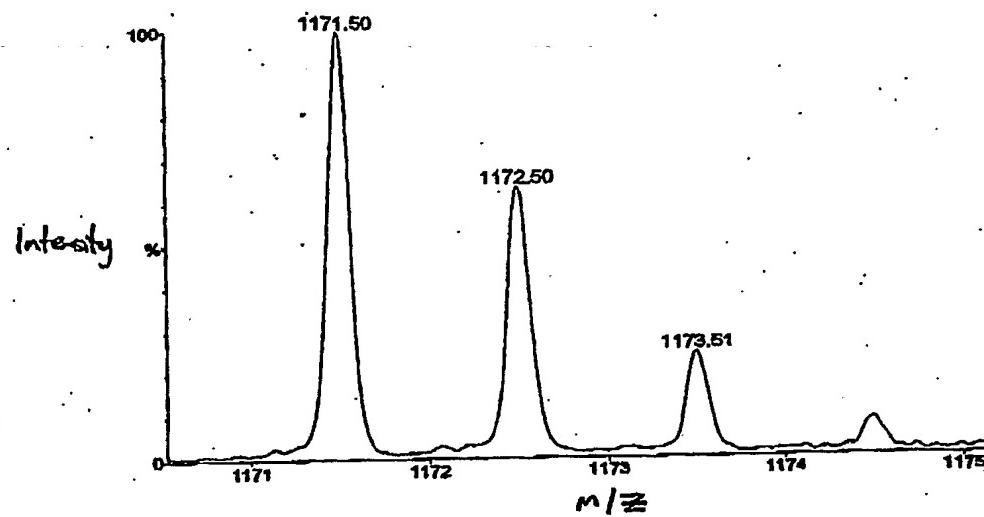


Fig. 15A

16/16

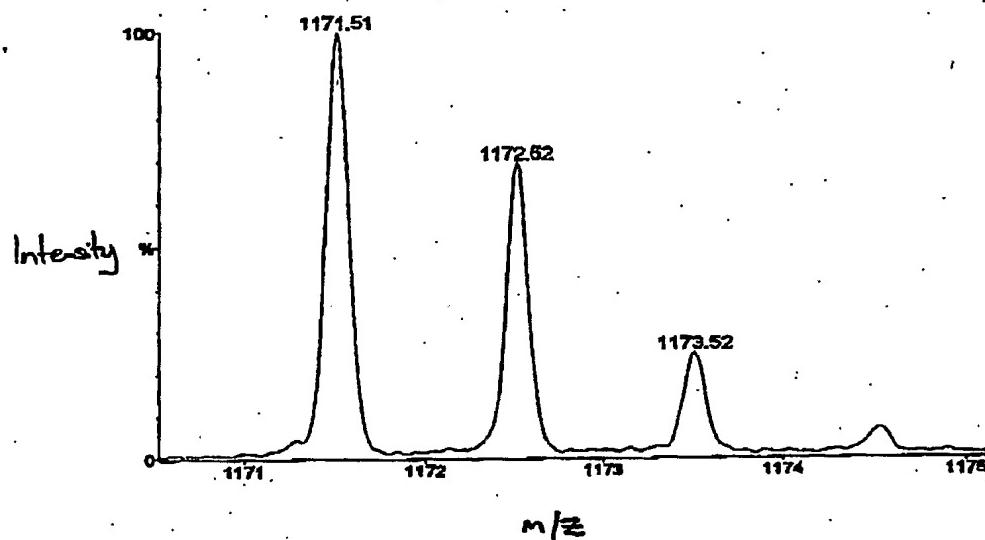


Fig. 15B